REMARKS

Claims 1, 6-10, and 16 are pending and stand rejected, and claims 11-15 and 17-44 stand withdrawn. Claim 1 is amended herein to recite a purified mature BNP2 polypeptide comprising an amino acid sequence having at least 85% sequence identity to the amino acid sequence of SEQ ID NO:1. Claims 6 and 8 are amended for consistency with amended claim 1, and claims 7 and 9 are cancelled without prejudice. In addition, claim 16 is amended to recite the language of claim 1. Support for these amendments can be found in Applicants' specification at, for example, page 8, line 25 to page 9, line 7. Thus, no new matter has been added.

In light of these amendments and the following remarks, Applicants respectfully request reconsideration and allowance of claims 1, 6, 8, 10, and 16.

Rejections under 35 U.S.C. § 112

The Examiner rejected claims 1, 6-9, and 16 under 35 U.S.C. § 112, first paragraph, alleging that they lack enablement. The Examiner asserted that Applicants' specification is enabling for a purified polypeptide comprising SEQ ID NO:3 or SEQ ID NO:36, but alleged that it does not reasonably provide enablement structurally or functionally for a polypeptide comprising SEQ ID NO:1 or a sequence that is 85% to 95% identical to SEQ ID NO:1. The Examiner further alleged that although the specification discloses upregulated expression of SEQ ID NOS:3 and 36 in heart tissue from heart failure patients, the specification does not show that the recited variant polypeptides or fragments are also upregulated, and that it is unpredicatable whether all of the claimed variant polypeptides and fragments are useful as diagnostic markers. The Examiner concluded by alleging that "the skilled artisan cannot contemplate how to use the claimed genus of polypeptides except SEQ ID NO:3 and 36." Office Action at page 6.

Applicants respectfully disagree. To further prosecution, however, Applicants have amended claim 1 herein to recite a purified mature BNP2 polypeptide comprising an amino acid sequence having at least 85% sequence identity to the amino acid sequence of SEQ ID NO:1. The present claims are fully enabled. This is particularly true given that Applicants' specification discloses methods for making BNP and using BNP polypeptides, including the mature BNP2 polypeptide set forth in SEQ ID NO:36. For example, Applicants' specification discloses how to construct nucleic acid sequences encoding BNP polypeptides, how to obtain

BNP polypeptides, how to use BNP polypeptides diagnostically and therapeutically, and how to detect BNP polypeptides. *See*, e.g., the sections of Applicants' specification extending from page 8, line 17 to page 9, line 19, from page 11, line 26 to page 12, line 21, and from page 20, line 29 to page 29, line 18, as well as Examples 5, 6, and 10. Further, Applicants' disclosure provides sufficient guidance with respect to amino acid substitutions and variants within SEQ ID NO:1. *See*, e.g., Applicants' specification at page 12, line 22 to page 13, line 10, which discloses the C-terminal amino acid sequences that are present in BNP2 from multiple different animal species as compiled in the amino acid sequence set forth in SEQ ID NO:20. A person having ordinary skill in the art, reading Applicants' specification at the time of its priority date, would have understood that the methods disclosed therein with respect to a polypeptide such as human BNP2 can be performed for any polypeptide recited in the present claims. As such, no undue experimentation would have been required to make and use a polypeptide as recited in the present claims, and the present claims are fully enabled.

In light of the above, Applicants respectfully request withdrawal of this rejection of claims 1, 6, 8, and 16 under 35 U.S.C. § 112, first paragraph.

The Examiner also rejected claims 1, 6-9, and 16 under 35 U.S.C. § 112, first paragraph, alleging that they fail to comply with the written description requirement. In particular, the Examiner alleged that the specification fails to teach the function of SEQ ID NO:1 or described other related proteins with limited homology, and does not teach what specific common structures can or cannot be changed or included in the claimed variants of SEQ ID NOS:1, 3, and 36 to preserve the activity of SEQ ID NOS:3 and 36. The Examiner concluded by alleging that Applicants were not reasonably in possession of the claimed genus of polypeptides.

Applicants respectfully disagree. To further prosecution, Applicants have amended claim 1 herein to recite a purified mature BNP2 polypeptide comprising an amino acid sequence having at least 85% sequence identity to the amino acid sequence of SEQ ID NO:1. The present claims are sufficiently described. For example, Applicants' specification sets forth SEQ ID NO:36, which is a mature BNP2 polypeptide that includes SEQ ID NO:1. *See*, e.g., page 8, line 25 to page 9, line 7, as well as Figure 1A. Applicants' specification also discloses examples of modifications that can be made within SEQ ID NO:1. *See*, e.g., SEQ ID NO:20 at page 12, line

22 to page 13 line 10, which represents a compilation of the C-terminal amino acid sequences that are present in BNP2 from multiple different animal species, including SEQ ID NO:1 from human BNP2. Applicants' specification also discloses how to determine the percent identity between two amino acid sequences. *See*, page 9, line 20 to page 11, line 6. Thus, Applicants' specification sets forth a representative number of species for the polypeptides recited in the present claims. As such, a person having ordinary skill in the art at the time of Applicants' priority date would have understood that Applicants invented and were in possession of the presently recited polypeptides.

In light of the above, Applicants respectfully request withdrawal of this rejection of claims 1, 6, 8, and 16 under 35 U.S.C. § 112, first paragraph.

In addition, the Examiner rejected claims 1, 6-10, and 16 under 35 U.S.C. § 112, first paragraph, alleging that they fail to comply with the written description requirement. The Examiner alleged that Applicants' specification does not provide support for the phrase "at least seven contiguous residues in length" in parts (b) and (d) of claim 1, and in claims 7 and 9.

Without acquiescing to the Examiner's rejection, Applicants have cancelled claims 7 and 9 herein without prejudice, and have amended claim 1 such that it does not include the rejected phrase. Thus, this rejection is moot.

Rejections under 35 U.S.C. § 102

The Examiner maintained the rejection of claims 1, 7, 9, and 16 under 35 U.S.C. § 102(e), alleging that they are anticipated by U.S. Patent No. 6,812,339 (the Venter et al. patent). In particular, the Examiner asserted that SEQ ID NO:7086 of the Venter et al. patent contains an amino acid fragment that has at least 85% identity to a fragment of SEQ ID NO:1 at least seven amino acids in length. The Examiner's reasoning was that 85% of seven residues is 5.95 residues, and SEQ ID NO:7086 includes a six amino acid fragment that is 100% identical to a fragment of present SEQ ID NO:1.

Applicants respectfully disagree. To further prosecution, however, Applicants have amended claim 1 to recite a purified mature BNP2 polypeptide comprising an amino acid sequence having at least 85% sequence identity to the amino acid sequence of SEQ ID NO:1. At

no point does the Venter et al. patent disclose such a polypeptide. The Venter et al. patent discloses nearly 6000 transcript sequences, as well as polypeptide sequences encoded by the transcripts, and genomic sequences associated with the transcripts. The Venter et al. patent also appears to disclose thousands of "context sequences" that flank single nucleotide polymorphisms within the transcript sequences. The Venter et al. patent does not, however, appear to disclose a purified mature BNP2 polypeptide comprising an amino acid sequence having at least 85 percent identity to the amino acid sequence of SEQ ID NO:1, as recited in the present claims. As such, the Venter et al. patent does not anticipate the present claims.

In light of the above, Applicants respectfully request withdrawal of this rejection of claims 1 and 16 under 35 U.S.C. § 102(e).

The Examiner also rejected claims 1, 7, 9, and 16 under 35 U.S.C. § 102(e), alleging that they are anticipated by U.S. Patent No. 6,887,481 (the Chan et al. patent). The Examiner asserted that the Chan et al. patent discloses SEQ ID NO:2, which comprises at least seven amino acids of present SEQ ID NO:1 and has at least 85-95% identity to a fragment of present SEQ ID NO:1.

Again, to further prosecution, Applicants have amended claim 1 to recite a purified mature BNP2 polypeptide comprising an amino acid sequence having at least 85% sequence identity to the amino acid sequence of SEQ ID NO:1. The Chan et al. patent fails to disclose such a polypeptide. Neither SEQ ID NO:2 or any other amino acid sequence set forth by Chan et al. comprises the sequence of a mature BNP2 polypeptide comprising an amino acid sequence having at least 85% sequence identity to SEQ ID NO:1. Thus, the Chan et al. patent fails to anticipate the present claims.

In light of the above, Applicants respectfully request withdrawal of this rejection of claims 1 and 16 under 35 U.S.C. § 102(e).

Information Disclosure Statement

Applicants note that an Information Disclosure Statement (IDS) was filed on August 25, 2006. As noted in the Amendment and Reply filed on January 5, 2009, Applicants respectfully request the Examiner to return an initialed copy of the Form PTO-1449 that accompanied the

IDS. A copy of the Form PTO-1449 is attached for the Examiner's convenience, as is a copy of the Return Receipt postcard that was received from the USPTO.

CONCLUSION

Applicants submit that claims 1, 6, 8, 10, and 16 are in condition for allowance, which action is respectfully requested. The Examiner is invited to telephone the undersigned agent if such would further prosecution

Please apply $245 for the extension of time fee, $405 for the Request for Continued Examination fee, and any other charges or credits, to deposit account 06-1050.

Respectfully submitted,

Date: October 23, 2009

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